III. REMARKS

Preliminary Remarks

Reconsideration and allowance of the present application based on the foregoing amendment and following remarks are respectfully requested. Claims 9-15 are currently pending and remain at issue.

On page 2 of the specification, the examiner objected to the specification with regard to the status of the parent application, which has matured into a US patent. In addition, the examiner has requested a description of Figures 1 and 2. The applicants have amended the priority information on page 1 of the specification and provided descriptions for Figures 1 and 2. Support for the description of Figures 1 and 2 can be found throughout the specification, for example, on pages 10 and 11, and on page 13, lines 1-4.

On pages 2 and 3 of the official action, the examiner alleged the applicants have failed to identify nucleotide sequence of at least 10 nucleotides and amino acids sequences of at least 4 amino acids in the specification by a proper sequence identifier according to 37 C.F.R. §§ 1.821 through 1.825. In particular, on pages 8 and 10 of the specification, three oligonucleotide sequences lacked SEQ ID NOS. Copies of the Sequence Listing in paper form and computer readable form for the above-identified application are attached hereto, in compliance with 37 C.F.R. §§ 1.821-1.825.

Pursuant to 37 C.F.R. §1.821(f) and (g), the applicants, through the undersigned attorney, hereby state that the sequence listing information of the attached copies of the Sequence Listing in paper and computer readable form are the same and do not contain new matter.

The applicants do not intend by these or any amendments to abandon subject matter of the claims as originally filed or later presented, and reserve the right to pursue such subject matter in a continuing application.

Patentability Remarks

Rejection Under 35 U.S.C. §112. Second Paragraph

On pages 3 and 4 of the official action, the examiner rejected claims 9-15 under 35 U.S.C. §112, second paragraph, for allegedly being indefinite. Specifically, the examiner asserted that the method claims are incomplete and omit essential steps such as the identification of the specific substrates and contacting the enzyme with the substrates under

appropriate conditions such that the required products are produced. The examiner also alleged that claim 12 was indefinite because it was not clear what enzymes or chemical methods racemize the hydantoins.

Solely for the purpose of expediting prosecution, and without prejudice to the applicants' right to seek broader claims in a continuing application, the applicants have canceled claims 9-15 without prejudice, thereby obviating the rejection of these claims. New claim 16 is directed to a method for production of a L-amino acid derived from a beta-aryl-substituted L-amino acid comprising (a) fermenting an *E.coli* host cell that contains an isolated polynucleotide selected from the group consisting of (i) a nucleotide sequence as set forth in SEQ ID NO: 1 and (ii) a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 2, (b) expressing an *Arthrobacter aurescens*' L-N-carbamoylase from step (a), and (c) contacting the L-N carbamoylase with N-carbamoyl or N-formyl amino acids to produce said L-amino acid derived from a beta-aryl-substituted L-amino acid. Support for new claim 16 can be found throughout the specification, for example, Table 1; page 9, lines 19-26; and page 11. New claim 16 specifically addresses the examiner's concerns regarding possible omitted steps in the claimed method.

Claims 17-21 are ultimately dependent upon claim 16 and thus contain the same essential steps for the method for production of a L-amino acid derived from a beta-aryl-substituted L-amino acid using the *Arthrobacter aurescens*' *hyu*C gene as set forth in SEQ ID NO: 1. Support for claims 17-21 can be found throughout the specification, for example, on page 5, lines 21-23 and page 17, lines 12-20. In view of the foregoing amendments and remarks, the applicants respectfully submit the rejection of claims 9-15 under 35 U.S.C. §112, second paragraph, is moot, and a rejection of new claims 16-21 on the same grounds would be improper.

Rejection Under 35 U.S.C. §112, First Paragraph

Enablement

On pages 4-7 of the official action, the examiner rejected claims 9-15 under 35 U.S.C. §112, first paragraph, for lacking enablement. Specifically, the examiner alleged that while the specification provides for a method of producing L-amino acids such as L-tryptophan, L-phenylalanine, and L-tyrosine by using the specific L-N-carbamoylase from *Arthrobacter aurescens* encoded by the polynucleotide sequence of SEQ ID NO: 1 (and encoded by the

amino acid sequence of SEQ ID NO: 2), the specification fails to provide a method of producing any or all L-amino acids using any carbamoylase enzyme from any source including variant mutants and recombinants. Furthermore, the examiner asserted that the specification fails to provide an enabling disclosure for a method of producing L-amino acids wherein the N-carbamoyl amino acids are produced with hydantoinases from corresponding hydantoins, which are racemized by enzymes or chemical methods. The examiner concluded that there is insufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonable correlated with the scope of the claims.

As discussed above, claims 9-15 have been canceled thereby obviating the enablement rejection of these claims. Furthermore, claim 16 is directed to method of producing L-amino acids as discussed above. The production of the specific L-amino acids derived from a beta-aryl-substituted L-amino acid is supported on page 11, lines 11-21, by L-N-carbamoylase is described in the specification at page 11, lines 11-21 and Table 1. As acknowledged by the examiner, the method of producing L-amino acids L-tryptophan, L-phenylalanine, and L-tyrosine from a beta-aryl-substituted L-amino acid is enabled by the specification. Specifically, the specification discloses and enables one of skill in the art to react the beta-aryl-substituted L-amino acid N-carbamoyl-L-thienylalanine with the recombinantly expressed *Arthrobacter aurescens*' L-N-carbamoylase to produce L-thienylalanine as well. [See Table 1] The applicants submit that the specification provides ample examples of *Arthrobacter aurescens*' L-N-carbamoylase converting a beta-aryl-substituted L-amino acid into its appropriate L-amino acid end product (*i.e.,* L-tryptophan, L-phenylalanine, L-tyrosine). As discussed above, claims 17-21 are ultimately dependent upon claim 16 and thus contain the same essential steps for the method for production of an L-amino acid derived from a beta-aryl-substituted L-amino acid using the *Arthrobacter aurescens*' *hyu*C gene as set forth in SEQ ID NO: 1.

New claim 22 is directed to a method for production of L-methionine comprising (a) fermenting an *E.coli* host cell that contains an isolated polynucleotide selected from the group consisting of (i) a nucleotide sequence as set forth in SEQ ID NO: 1; and (ii) a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 2, (b) expressing a specific encoded *Arthrobacter aurescens*' L-N-carbamoylase from step (a), and (c) contacting the L-N carbamoylase with N-carbamoyl-L-thienylalanine to produce L-thienylalanine. Support for claim 22 can be found throughout the specification, for example, page 11, lines 11-21 and Table 1. The applicants respectfully submit the L-N-carbamoylase enzyme also converted N-

carbamoyl-L-methionine to L-methionine as indicated in Table 1, page 12. Claims 23-27 are ultimately dependent upon claim 22 and thus contain the same essential steps for the method for production of L-methionine, using the *Arthrobacter aurescens*' *hyu*C gene as set forth in SEQ ID NO: 1. In view of the foregoing amendments and remarks, the applicants respectfully request that the rejection of claim 9-15 under 35 U.S.C. §112, first paragraph, for lack of enablement is moot, and a rejection of new claims 16-27 on the same grounds would be improper.

Written Description

On pages 9-13 of the official action, the examiner rejected claims 9-15 under 35 U.S.C. §112, first paragraph, for lacking proper written descriptive support. Specifically, the examiner alleged that no information beyond the characterization of SEQ ID NO: 2 has been provided by the applicants that would indicate they were possession of the genus of modified polypeptides for use in the claimed method. The examiner also alleged that claims 11 and 12 lacked proper written descriptive support because the specification does not contain any disclosure of the structure of all polypeptide sequences, including fragments and variants within the scope of the claimed method.

As discussed above, claims 9-15 have been canceled without prejudice. Claims 16-27 are directed to the claimed methods as described above wherein either the use of the polynucleotide set forth in SEQ ID NO: 1, or the encoded amino acid sequence as set forth in SEQ ID NO: 2 is used to produce either an L-amino acid derived from a beta-aryl substituted L-amino acid or L-methionine. These claims are fully supported throughout the specification. In view of the foregoing amendments, the applicants respectfully request the rejection of claims 9-15 under 35 U.S.C. §112, first paragraph, for lack of written description, is now moot, and a rejection of new claims 16-27 on the same grounds would be improper.

Rejection Under 35 U.S.C. §102(b)

On pages 13 and 14 of the official action, the examiner rejected claims 9-12 under 35 U.S.C. §102(b) as being anticipated by either U.S. Patent No. 5,516,660 (hereafter the '660 patent) or Gross *et al., J. Biotechnol.* 14:363-375 (1990) (hereafter Gross *et al.*). The examiner alleged that Gross *et al.* and the '660 patent disclose an identical method of using the carbamoylase produced by *A. aurescens* wherein N-carbamoyl or N-formyl amino acids

are reacted and wherein said N-carbamoyl or N-formyl amino acids are produced by hydantoinases from corresponding hydantoins racemized by enzymatic or chemical methods.

As discussed above, claims 9-12 have been canceled without prejudice. New claims 16 and 22 are directed to a method for production of an L-amino acid derived from a beta-aryl-substituted L-amino acid or L-methionine comprising **fermenting an E. coli host cell** that contains an isolated polynucleotide selected from the group consisting of (i) a nucleotide sequence as set forth in SEQ ID NO: 1 (nucleotide sequence of *hyu*C gene from *Arthrobacter aurescens*) and (ii) a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 2, producing a specific encoded Arthrobacter aurescens L-N-carbamoylase, and contacting the L-N carbamolyase with N-carbamoyl or N-formyl amino acids (beta-aryl-substituted or L-methionine based) to produce said L-amino acids. Neither Gross et al. or the '660 patent teach the methods as described above **using the unique polynucleotide sequences (*i.e.*, SEQ ID NOS: 1 and 2 *hyu*C gene from *Arthrobacter aurescens*) in a recombinant manner in *E. coli*** for fermentation of an L-amino acid derived from a beta-aryl substituted L-amino acid or L-methionine.

In view of the foregoing amendments and remarks, the applicants respectfully submit that the rejection of claims 9-12 under 35 U.S.C. §102(b) is moot, and a rejection of new claims 16-27 would be improper.

Rejection Under 35 U.S.C. §103(a)

On pages 14 and 15 of the official action, the examiner rejected claims 13-15 under 35 U.S.C. §103(a) as being unpatentable over Gross *et al.* or the '660 patent in view of common knowledge regarding immobilization of enzymes. The examiner asserted that while the references teach the method of making L-amino acids using the enzyme, the references are silent as to the use of enzyme immobilization technique for the same. The examiner alleged, however, that the technique of immobilizing the enzyme onto a solid support and use of such columns in continuous production of enzyme products is well known in the art. Thus, the examiner concluded that one of skill would have known, been motivated and had reasonable expectation of success to immobilize the carbamoylase enzyme onto a solid support to lower production costs of L-amino acids.

As discussed above, claims 13-15 have been canceled without prejudice. New claims 17, 18, 23, and 24 are directed to the claimed methods of either claim 16 or 22 as discussed

above, further comprising immobilizing L-N-carbamoylase covalently onto carriers such as EAH-sepharose.

With regard to the primary references, Gross *et al.* teach the reaction parameters and stereospecificity of L,N-carbamoylase directly isolated from *Arthrobacter*. The '660 patent teaches the use and method of producing particular L-amino acids using particular *Arthrobacter* strains. Neither Gross *et al.* nor the '660 patent fail to teach or suggest using *E.coli* to express the recombinant *Arthrobacter aurescens'* L-N-carbamoylase gene as set forth in SEQ ID NO: 1 in order to produce L-tryptophan, L-phenylalanine, L-thienylalanine, L-tyrosine and L-methionine.

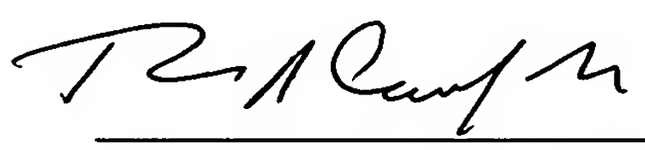
With regard to common knowledge of immobilizing the enzyme on a solid support, the applicants respectfully submit that this knowledge does nothing to overcome the failings of the primary documents. Specifically, common knowledge alone or in combination with Gross *et al.* or the '660 patent do not teach methods of fermenting L-amino acids derived from a beta-aryl substituted L-amino acid or L-methionine using the specific recombinant *hyu*C gene from *Arthrobacter aurescens*' as set forth in SEQ ID NO: 1. Accordingly, the applicants respectfully submit one of skill in the art would not find a method for production of an L-amino acid derived from a beta-aryl substituted L-amino acid or L-methionine comprising (a) fermenting an *E.coli* host cell that contains an isolated polynucleotide selected from the group consisting of (i) a nucleotide sequence as set forth in SEQ ID NO: 1 and (ii) a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 2, (b) producing a specific encoded *Arthrobacter aurescens*' L-N-carbamoylase from step (a), and (c) contacting the L-N carbamoylase with N-carbamoyl or N-formyl amino acids to produce said L-amino acids wherein the isolated L-N-carbamoylase is immobilized onto a carrier in view of common knowledge, or the teachings or suggestions of either Gross *et al.* or the '660 patent.

Accordingly, without such teaching or suggestion, the examiner would not establish a prima facie case of obviousness for new claims 13-15. In view of the foregoing amendments and remarks, the applicants respectfully submit the rejection of claims 13-15 under 35 U.S.C. §103(a) over Gross *et al.* and the '660 patent in view of common knowledge regarding immobilization of enzymes is moot, and a rejection of new claims 17, 18, 23, and 24 would be improper.

III. CONCLUSION

In view of the foregoing, the applicants respectfully submit that this application is in condition for allowance. A timely notice to that effect is respectfully requested. If questions relating to patentability remain, the examiner is invited to contact the undersigned to discuss those questions.

Respectfully submitted,
PILLSBURY WINTHROP LLP



Thomas A. Cawley, Jr., Ph.D.
Reg. No. 40,944
Tel. No. 703-905-2144
Fax No. 703-905-2500

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TAC/PAJ
P.O. Box 10500
McLean, VA 22102
(703) 905-2000